

	IL-1 Hy2	IL-1 Hy1	rat IL-1Ra	pig IL-1Ra	Hu sIL-1Ra	Hu icIL-1Ra
1	M	M	M	M	M	M
1	V	E	E	E	E	A
1	L	I	I	I	I	L
1	S	C	C	C	C	S
1	G	R	R	R	R	G
1	A	P	P	P	P	A
1	L	C	C	C	C	L
1	C	S	S	S	S	C
1	S	H	H	H	H	S
1	L	I	I	I	I	L
1	P	L	L	L	L	P
1	M	S	S	S	S	M
1	A	R	R	R	R	A
1	R	I	I	I	I	R
1	Y	L	L	L	L	Y
1	I	L	L	L	L	I
1	K	F	F	F	F	K
1	Y	R	R	R	R	Y
1	-	S	S	S	S	-
1	-	E	E	E	E	-
1	-	T	T	T	T	-
1	-	I	I	I	I	-
1	-	C	C	C	C	-
1	-	R	R	R	R	-
1	-	P	P	P	P	-
1	-	C	C	C	C	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-
1	-	K	K	K	K	-
1	-	S	S	S	S	-
1	-	S	S	S	S	-

15	-	-	-	A	D	Q	K	A	L	Y	T	R	D	G	Q	L	L	V	G	D	P	V	A	D	N	C	C	-	A	E	K	I	C	T	L	P	N	R	G	L	IL-1 Hy2
11	M	K	D	S	A	L	K	V	L	Y	L	H	N	N	Q	L	L	A	G	L	H	A	G	K	V	I	K	G	E	E	I	S	V	V	P	N	R	W	L	IL-1 Hy1	
41	I	W	D	T	N	Q	K	T	F	Y	L	R	N	N	Q	L	L	A	G	Y	L	Q	G	P	N	T	K	L	E	E	K	I	D	M	V	P	-	-	-	-	rat IL-1Ra
40	I	W	D	V	N	Q	K	T	F	Y	L	R	N	N	Q	L	V	A	G	Y	L	Q	G	P	N	T	K	L	E	E	K	I	D	V	V	P	-	-	-	-	pig IL-1Ra
40	I	W	D	V	N	Q	K	T	F	Y	L	R	N	N	Q	L	V	A	G	Y	L	Q	G	P	N	V	N	L	E	E	K	I	D	V	V	P	-	-	-	-	Hu sIL-1Ra
22	I	W	D	V	N	Q	K	T	F	Y	L	R	N	N	Q	L	V	A	G	Y	L	Q	G	P	N	V	N	L	E	E	K	I	D	V	V	P	-	-	-	-	Hu icIL-1Ra

IL-1 Hy2	IL-1 Hy1	rat IL-1Ra	pig IL-1Ra	Hu sIL-1Ra	Hu icIL-1Ra
51	51	77	76	76	58
D	D	-	-	-	-
R	A	I	V	I	I
T	S	D	E	E	E
K	L	F	P	P	P
V	P	N	H	H	H
I	V	V	V	A	A
F	I	F	F	L	L
L	L	L	L	L	L
G	G	G	G	G	G
I	V	I	I	I	I
Q	Q	H	H	H	H
G	G	G	G	G	G
S	S	K	K	K	K
R	Q	L	L	M	M
C	C	C	C	C	C
L	L	L	L	L	L
A	S	S	S	S	S
C	C	C	C	C	C
V	G	V	V	V	V
E	-	K	K	K	K
T	V	S	S	S	S
E	G	G	G	G	G
E	Q	D	D	D	D
G	E	E	E	E	E
P	P	T	M	T	T
S	T	K	K	R	R
L	L	L	L	L	L
Q	T	Q	Q	Q	Q
L	L	L	L	L	L
E	E	E	A	A	A
E	M	T	V	V	V
L	L	N	N	N	N
Y	Y	N	N	S	S

91	K	G	E	A	T	R	F	T	F	F	Q	S	S	S	G	S	A	F	R	L	E	A	A	W	P	G	W	F	L	C	G	P	A	E	P	Q	Q	IL-1 Hy2		
90	L	G	A	K	E	S	K	S	F	T	F	Y	R	R	D	M	G	L	T	S	S	F	S	A	A	P	G	W	F	L	C	T	V	P	E	A	D	Q	IL-1 Hy1	
116	K	N	K	E	D	K	R	F	T	F	I	R	S	E	T	G	P	T	T	S	S	F	L	A	C	P	G	W	F	L	C	T	T	L	E	A	D	H	rat IL-1Ra	
115	K	N	S	E	D	K	R	F	T	F	I	R	S	D	S	G	P	T	T	S	S	F	S	A	A	C	P	G	W	F	L	C	T	A	L	E	A	D	Q	pig IL01Ra
115	E	N	R	K	D	K	R	F	A	F	I	R	S	D	S	G	P	T	T	S	S	F	S	A	A	C	P	G	W	F	L	C	T	A	M	E	A	D	Q	Hu sIL-1Ra
97	E	N	R	K	D	K	R	F	A	F	I	R	S	D	S	G	P	T	T	S	S	F	S	A	A	C	P	G	W	F	L	C	T	A	M	E	A	D	Q	Hu icIL-1Ra

**Fig. 1A**

131	P	V	Q	L	T	K	E	S	E	P	S	A	R	-	-	-	-	T	K	F	Y	F	E	Q	S	W
130	P	V	R	L	T	Q	L	P	E	N	G	G	W	N	A	P	I	T	D	F	Y	F	Q	Q	C	D
156	P	V	S	L	T	N	T	P	K	E	P	-	-	-	C	T	V	T	K	F	Y	F	Q	E	D	Q
155	P	V	G	L	T	N	T	P	K	A	A	-	-	-	V	K	V	T	K	F	Y	F	Q	Q	D	Q
137	P	V	S	L	T	N	M	P	D	E	G	-	-	-	V	M	V	T	K	F	Y	F	Q	E	D	E
137	P	V	S	L	T	N	M	P	D	E	G	-	-	-	V	M	V	T	K	F	Y	F	Q	E	D	E

IL-1 Hy2

IL-1 Hy1

rat IL-1Ra

pig IL-1Ra

Hu sIL-1Ra

Hu icIL-1Ra

IL-1 Hy2  
 IL-1 Hy1  
 rat IL-1Ra  
 pig IL-1Ra  
 Hu sIL-1Ra  
 Hu icIL-1Ra

Decoration 'id-consensus': Box residues that match the Consensus exactly.

Fig.1B

FIGURE 2A

SEQ ID NO.: 12

```

10      20      30      40      50      60
GGCAGTGGGA CTGGGTTTGA GCTGGGCTTA TCCTCCAAC TGTGAGGAGG CTACAGCACA 60
CTCCACCCCA CTCTCAGGGC TGGGAATTGT TGTGGCTCAG CTATTTTGGG GAATCTGTTT 120
TCCAGTTTCT CAGAACCCAGC GCAAGCACAC ACATCCCAGG CTCACACCCC TGGTGGCTGG 180
ACTTGCTCCC GGATAGCCTC AGTCAGGGAG AGGCAGAGCT GCCTGGAGCC TGTGGGCTG 240
GTGGAAGCCT TGGTGGATT C TGGCAGGCCA ATTATAGATG AATGGCCTGG GGAACCCGTG 300

310      320      330      340      350      360
CAGCCCGTGG CTGAGTGGTT CTAAGCCCCA GCACGTCTGC CTCGGCTTC ACCAGCCTC 360
CTTTTCTAAC TGCCCTTCTC TCCTCCCCAT CAGTGAGGAC CAGACACCAC TGATTGCAGG 420
AATGTGTTCC CTCCCCTATG CAAGATACTA CATAATTAAA TATGCAGACC AGAAGGCTCT 480
ATACACAAGA GACGGCCAGC TGCTGGTGGG AGATCCTGTT GCAGACAACT GCTGTGCAGA 540
GAAGATCTGC ACACTTCCCTA ACAGAGGCTT GGACCGCACC AAGTCCCCA TTTTCTGGG 600

610      620      630      640      650      660
GATCCAGGGA GGGAGCCGCT GCCTGGCATG TGTGGAGACA GAAGAGGGGC CTTCCTTACA 660
GCTGGAGGAT GTGAACATTG AGGAACGTGA CAAAGGTGGT GAAGAGGCCA CACGCTTCAC 720
CTTCTTCCAG AGCAGCTCAG GCTCCGCCCT CAGGCTTGAG GCTGCTGCCCT GGCCCTGGCTG 780
GTTCCCTGTG GTCCCGGCAG AGCCCCAGCA GCCAGTACAG CTCACCAAGG AGAGTGAGCC 840
CTCAGCCCGT ACCAAGTTT ACTTTGAACA GAGCTGGTAG GGAGACAGGA AACTGCCGTT 900
```

FIGURE 2B

910	920	930	940	950	960
TAGCCTTG	CCCCCAACC	AAGCTCATCC	TGCTCAGGGT	CTATGGTAGG	CAGAAATAATG
TCCCCCGAA	TATGTCCACA	TCCTAATCCC	AAGATCTGTG	CATATGTTAC	CATACATGTC
CAAAGAGGTT	TTGCAAAATGT	GATTATGTTA	AGGATCTTGA	AATGAGGAGA	CAATCCTGGG
TTATCCTTGT	GGGCTCAGTT	TAATCACCAAG	AAGGAGGCAG	GAAGGGAGAG	TCAGAGAGAG
AATGGAAGAT	ACCATGCTTC	TAAATTTTGA	GATGGAGTGA	GGGGCCTTGA	GCCAACATAT
1210	1220	1230	1240	1250	1260
GCTTGTGTTT	TTAGAAGGAG	GAAAAGCCAA	GGGAACGGAT	TCTCCTCTAT	AGTCTCCGGA
AGGAACACAG	CTCTTGACAC	ATGGATTTC	GCTCAGTGAC	ACCCATTTC	GACTTCTGAC
CTCCACAAC	ATAAAATAAT	AAACTTGTGT	TATTGTAAAC	CTCTGG	1366

FIGURE 3

SEQ ID NO.: 13

10	20	30	40	50
MNGLGNPCSP	WLSGSKPQHV	CLWLHPASF	NCPSLLPISE	DQTPLIAGMC
SLPMARYYII	KYADQKALYT	RDGQLLVGDP	VADNCCAEKI	CTLPNRGLDR
TKVPIFLGIQ	GGSRCLACVE	TEEGPSLQLE	DVNIIEELYKG	GEEATRFTFF
QSSSGSAFRL	EAAAWPGWFL	CQPAEPQQPV	QLTKESEPSA	RTKFYFEQSW
				200

FIGURE 4A

SEQ ID NO.: 14

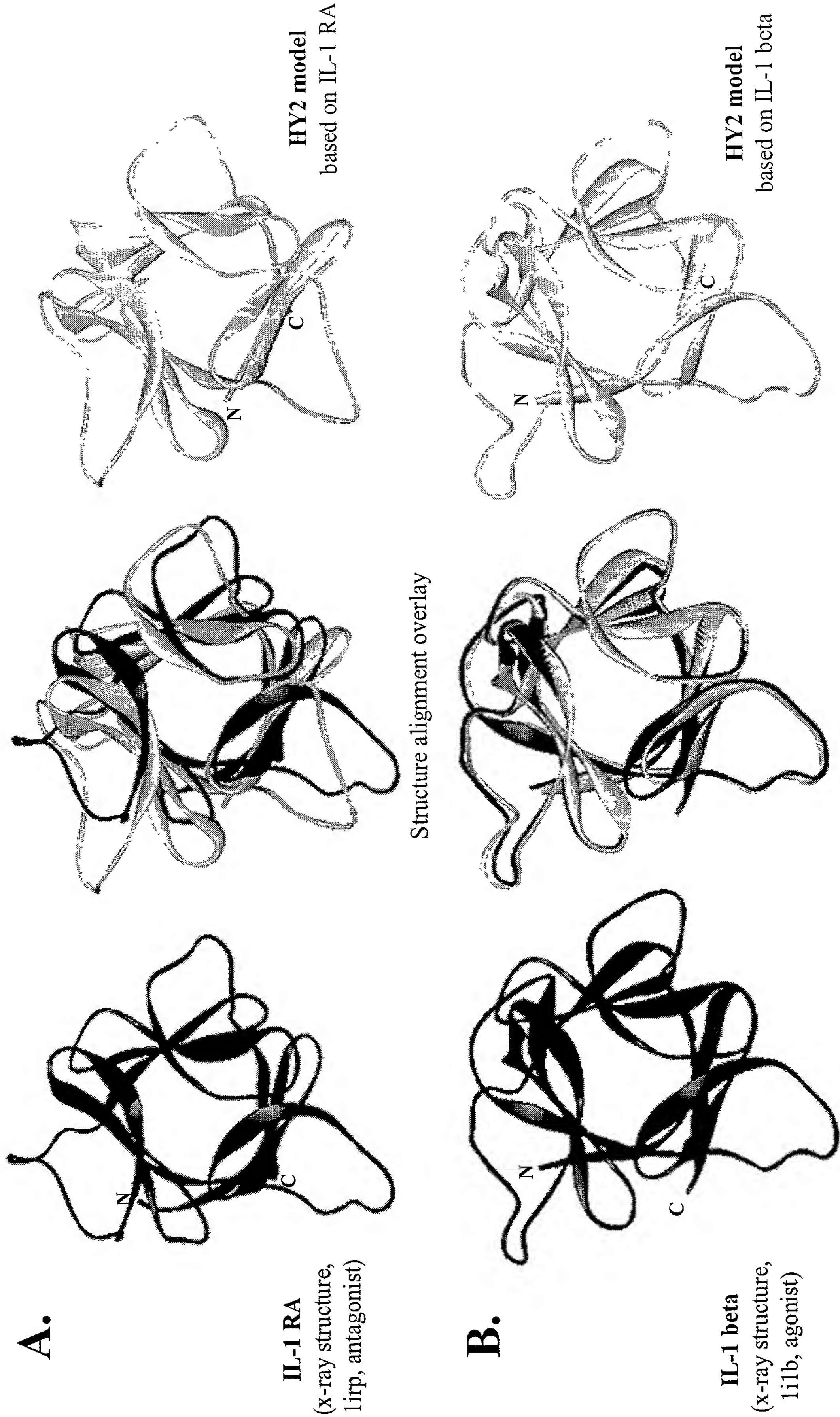
10	20	30	40	50	60
GGCAGTGGGA	CTGGGTTTGA	GCTGGGCTTA	TCCCTCCAAC	GTGAGGGAGG	CTACAGCACACA
CTCCACCCCA	CTCTCAGGGC	TGGGAATTGT	TGTGGCTCAG	CTATTGGGG	GAATCTGTTT
TCCAGTTTCT	CAGAACCCAGC	GCAAGCACAC	ACATCCCAGG	CTCACACCCC	TGGTGGCTGG
ACTTGCTCCC	GGATAGCCTC	AGTCAGGGAG	AGGCAGAGCT	GCCTGGAGCC	TGCTGGGCTG
GTGGAAGCCT	TGGTGGATT	TGGCAGGCCA	ATTATAGACG	AATGGCCTGG	GGAACCCCGTG
310	320	330	340	350	360
CAGCCCGTGG	CTGAGTGGTT	CTAAGCCCCA	GCACGTCTGC	CTCTGGCTTC	ACCCAGCCTC
CTTTTCTAAC	TGCCCTTCTC	TCCCTCCCCAT	CAGTGAGGAC	CAGACACCAC	TGATTGCAGG
AATGTGTTCC	CTCCCCATGG	CAAGATACTA	CATAATTAAA	TATGCAGACC	AGAAGGCTCT
ATACACAAGA	GACGGCCAGC	TGCTGGTGGG	AGATCCTGTT	GCAGACAACT	GCTGTGCAGA
GAAGATCTGC	ACACTTCCTA	ACAGAGGCTT	GGACCGCAC	AAGGTCCCCA	TTTTCTCTGGG
610	620	630	640	650	660
GATCCAGGGA	GGGAGCCGCT	GCCCTGGCATG	TGTGGAGACA	GAAGAGGGGC	CTTCCCTACA
GCTGGAGGAT	GTGAACATTG	AGGAACCTGT	CAAAGGTGGT	GAAGAGGCCA	CACGCTTCAC
CTTCTTCCAG	AGCAGCTCAG	GCTCCGCCCTT	CAGGCTTGAG	GCTGCTGCCCT	GGCCTGGCTG
GTTCCCTGTGT	GGCCCGGCAG	AGCCCCAGCA	GCCAGTACAG	CTCACCAAGG	AGAGTGAGCC
CTCAGCCCGT	ACCAAGTTTT	ACTTTGAACA	GAGCTGGTAG	GGAGACAGGA	AACTGCGTTT
					900

FIGURE 4B

910	920	930	940	950	960
TAGCCTTG TG	CCCCCAAACC	AAGCTCATCC	TGCTCAGGGT	CTATGGTAGG	CAGAAATAATG
TCCCCCGAAA	TATGTCCACA	TCCTAATCCC	AAGATCTGTG	CATATGTTAC	CATACATGTC
CAAAGAGGTT	TTGCAAATGT	GATTATGTTA	AGGATCTTGA	AATGAGGAGA	CAATCCTGGG
TTATCCTTGT	GGGCTCAGTT	TAATCACAAAG	AAGGAGGCAG	GAAGGGAGAG	TCAGAGAGAG
AATGGAAGAT	ACCATGCTTC	TAATTTTGAA	GATGGAGTGA	GGGGCCTTGA	GCCAACATAT
1210	1220	1230	1240	1250	1260
GCTTGTGTTT	TTAGAAGGAG	GAAAAGCCAA	GGGAACGGAT	TCTCCTCTAT	AGTCTCCGGA
AGGAACACAG	CTCTTGACAC	ATGGATTTCA	GCTCAGTGAC	ACCCATTTCA	GACTTCTGAC
CTCCACAAC T	ATAAAATAAT	AAACTTGTGT	TATTGTAAAC	CTCTGG	1366



Figure 5





Sequence Alignment based on 2° Structure

Figure 6

Hy2 and IL-1 RA (antagonist)

	----	1->	-2----	----	3----	--4-->	--5-->	
IL-1RA:	10	MQAFRIWDVNQKTFYLRNNQLVAGYLQGPVNLEEKIDVVPIEPHA	----	----	----	----	LFLGIHGK	64
		+ + I	+QK	Y R+	QL+ G	N	EKI ++P	+FLGI GG
Hy2	: 1	ARYYIIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLDRTKVP	IFLGIQGS	59				
		----	6----	----	7----	variable dom.	--8----	--9-->
								--10-->
IL-1RA:	65	MCLSCVKSGDETRLQLEAVNITDLSNRKQDKRFAFIRSDSGPTTSFESAACPGWFLCTA	124					
		CL+CV++ +	LQLE	VNI +L +	++	RF F +S	SG	E+AA PGWFLC
Hy2	: 60	RCLACVETEEGPSLQLEDVNIIEELYKGGEATRTFFQSSSGSAFRLEAAAWPGWFLCGP	119					
		----	11->	----	12----			
IL-1RA:	125	MEADQPVSLTNMPDEGMVTKFYFQEDE	152					SEQ ID NO: 21
		E	QPV	LT	E	TKFYF++		
Hy2	: 120	AEPQQPVLTKES-EPSARTKFYFEQSW	146					SEQ ID NO: 22

--β-strand-->

SEQ ID NO:22 = amino acid 7-153  
of SEQ ID NO: 2

# Sequence Alignment based on 2° Structure

# Sequence Alignment based on 2° Structure

Hy2 and IL-1 beta (agonist)

IL-1β: 3	VRSLNCTLRDSQQKSLVMSGPYELKALHLQGDMEQQVVFMSFVQGEESNDKIPVALGL 62	SEQ ID NO: 23
	+ ++ + QK+L +L + + + +G + K+P+ LG+	
Hy2 : 1	PMARYYIIKYADQKALYTRDG-QLLVGDPVADNCCA EK-ICILPNRGLDRT-KVPIFLGI 57	SEQ ID NO: 24
IL-1β: 63	KEKNLYLSCVLKDDKPTLQLESVDPKN-YPKKKMEKRFVFNKIEINNKLFEFSAQFPNWX 121	SEQ ID NO: 23
	+ + L+CV ++ P+LQLE V+ + Y + RF F + E+A +P W+	
Hy2 : 58	QGGSRCLACVETEEGPSLQLEDVNIEELYKGGEETRTFTFFQSSSGSAFRLEAAAWPGWF 117	SEQ ID NO: 24

[illegible]IL-1β: 122 ISTSQAENMPVFLGGTKGGQDITDFTMQFVSS 153  
SEQ ID NO: 23
$$+ \quad \text{PV L} \quad + \quad \text{T F} \quad +$$

Hy2 : 118 LCGPAEPQQPVQLTKESEPSARTKFFFEQSW 148

--β-strand-->

**SEQ ID NO: 24 = amino acid 5-153  
of SEQ ID NO: 2**